REMARKS/ARGUMENTS

Claims 38, 40-41, 46 and 48 are under examination. Claim 38 has been amended to better claim the subject matter which Applicants regard as the invention and for improved clarity. Support is found throughout the Specification, in particular, at page 5, line 14 and page 12, lines 7-13, and in the as-filed claims. Accordingly, no new matter has been added with the present Amendment.

Claim Rejection under 35 U.S.C. 112:

Claims 38, 40-41, 46 and 48 are rejected under section 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

However, without acquiescing to this rejection and in the interest of advancing prosecution of this case, claim 38 has been amended such that the method claimed is to inhibit, retard or kill a *Plasmodium* species in a host parasitized by the Plasmodium species. Claims 40-41, 46 and 48 are dependent claims of claim 38. Applicants submit that the claims as amended are fully enabled by the specification. Withdrawal of the rejection is respectfully requested.

Regarding the Examiner's assertion that the claims contain subject matter which was not described in the specification in such a way to enable one skilled in the art to make and/or use the invention, Applicants submit the following:

The present invention stemmed from the inventors' findings that the level of NO was inversely correlated with malaria disease severity in children (see Examples 1-8) and adults (see Examples 16-23). These results suggested that NO is likely to have a protective role in patients with malaria. These findings were surprising because this

field at the time has been confusing regarding the role of NO in malaria. The prevailing view was that NO mediates and contributes to pathology of severe malaria.

In order to establish that NO production can retard parasite growth, the inventors took advantage of a well established standard *in vitro* assay, called cytoadherence assay. Cytoadherence is fundamental for the survival of *Plasmodium* species *in vivo*. For this reason, the cytoadherence assay has been used in the art to study any effects on survival and virulence of the malarial parasite *Plasmodium*. As shown in Figs. 1 and 2 and described in Examples 13-15, the treatment of parasitized red blood cells with SNO-cysteine inhibited adherence properties thereof to C32 melanoma cells. SNO-cysteine is an example of the NO donors useful for the invention. The C32 melanoma cells are a human melanoma cell line. Therefore, these results clearly establish that an agent capable of increasing NO levels can be used to treat an infection caused by *Plasmodium* species.

The Office Action raises various issues regarding the "adequate clinical model" and the sufficiency of the "*in vitro* model" for the claimed invention.

As discussed above, Applicants maintain that the invention is sufficiently described in the specification to enable those skilled in the art to make and/or use the invention as claimed. The cytoadherence assay used in the present case is a well accepted standard *in vitro* assay in the art for studying *Plasmodium* life cycle. This is because the phenomenon of cytoadherence is essential for parasite survival and virulence. Accordingly, the data obtained from the cytoadherence assay are predictive of the in *vivo* situation. This is consistent with the provision in MPEP 2164.02 regarding the issue of correlation between *in vitro* or *in vivo* animal model assays and a claimed method of use ("....if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate...") (emphasis added).

Applicants further submit that the guidelines provided in the specification (pages 11 and 18-21) regarding the mode of administration, the dosage and etc. of the NO modifying agents useful for practicing the invention meet the requirements under the law for obtaining a patent. This is consistent with the court decision in Scott v. Finney 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed. Cir. 1994) ("Testing for the full safety and effectiveness of a prosthetic device is more properly left to the FDA. Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office proceedings").

Conclusion:

In view of the foregoing, it is submitted that this case is in condition for allowance, and passage to issuance is respectfully requested.

If there are further issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

It is believed that this submission does not require the payment of any fees. However, if this is incorrect, please charge any deficiency or credit any overpayment to Deposit Account No. 07-1969.

Respectfully submitted,

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